REMARKS

Reconsideration of the allowability of the present application in view of the above claim amendments and the following remarks is requested respectfully.

Discussion of the Claims

This responds to the Action dated May 18, 2007 and supplements the Examiner Interview dated October 3, 2007.

Claims 1, 2, 4, 5, 20, 23 to 34, 36 to 40, 45 to 51, and 55 to 66 were acted upon by the Examiner. Claims 1, 4, 5, 20, 23, 24, 26, 28 to 30, 33, 34, 36 to 40, 45, 47 to 51, 55 to 57, and 59 to 62 have been amended. Claims 2, 25, 31, 32, 46, 58, and 63 to 66 have been canceled. Claims 67 to 81 have been added. Accordingly, claims 1, 4, 5, 20, 23, 24, 26, 28 to 30, 33, 34, 36 to 40, 45, 47 to 51, 55 to 57, 59 to 62, and 67 to 81are presented for examination.

Discussion of the Amendments

Claims 1, 33, 47, 57, and 59 are independent claims. Claim 1 is directed to a SSRI composition comprising one or more quantities of particles. Claim 33 is directed to a method for the treatment of depression using the composition as described in claim 1. Claim 47 is directed to a SSRI composition comprising a first and a second quantity of particles. Claim 57 is directed to a method for the treatment of depression using the composition as described in claim 47. Claim 59 is directed to a unit dose formulation of an SSRI composition that provides certain blood levels of fluvoxamine.

Claims 23, 24, 28-30 are directed to different dissolution profiles of the SSRI composition. The subject matter of these claims have been added as dependent claims to claims 33, 47, and 59. They appear as claims 34 and 35, and new claims 69 to 81.

Claim 1 is reproduced below without revision marks showing the amendments. The claim below is annotated to show where the specification supports the substantive amendments to the claim. Other amendments to the claims were made to clarify that which the applicant's regard as the invention.

1. (Currently Amended) A multiparticulate

controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration, the multiparticulate composition comprising:

one or more quantities of particles [*Tables 8A and 8B, and accompanying description at pages 28 and 29*], each of the particles comprise

(i) an inert non-pareil core [*pg. 10, lns 19-24*],

(ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and

(iii) a rate-controlling membrane coating disposed over the SSRI layer,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration [*pg. 4, lns 6-13*].

Claim 47 is reproduced below without revision marks showing the amendments. The claim below is annotated to show where the specification supports the substantive amendments to the claim. Other amendments to the claims were made to clarify that which the applicant's regard as the invention.

47. (Currently Amended) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles[*Tables 8A and 8B, and accompanying description at pages 28 and 29*], each of the particles comprising

(i) an inert non-pareil core[*pg. 10, lns 19-24*],

(ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and

(iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration[*pg. 4, lns 6-13*], and

wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount [*Tables 8A, 8B, and 9, and accompanying description at pages 28-30*].

No new matter has been added.

I. Discussion of the Examiner's Section 103 Rejection of Claims 1, 2, 4, 5, 20, 25 to 27, 31 to 33, 36 to 40, 47 to 51, and 64 to 66

The Examiner rejected Claims 1, 2, 4, 5, 20, 25 to 27, 31 to 33, 36 to 40, 47 to 51, and 64 to 66 under 35 U.S.C. § 103(a) as being obvious over the disclosure of U.S. Patent No. 5,958,458 to Norling et al. in view of U.S. Patent No. 6,183,780 to van Balken et al. Applicants respectfully traverse the rejection.

Neither Norling et al. nor Van Balken et al. teach the claimed non-pareil core.

Applicants submit that neither Norling et al. nor van Balken et al alone or in combination teach or fairly suggest all of the limitations of the presently amended claims, particularly an inert, non-pareil core. Accordingly, a *prima facie* case of obviousness has not been established.

As noted in the present Action, Norling teaches particles with a core made from a specific material and having a unique property: a friability of at most 20% (Col. 2, lns. 22-32). These cores are taught by Norling et al. as having "a mechanical strength expressed by the means of friability (Col. 3, lns. 7-9) where friability is defined by a test using a Erweka apparatus (Col. 19, lns,25-54). Exemplary core materials that exhibit the desired friability described in Norling et al. are listed at Col. 5, lns, 9-15. Absent from such a list is the non-pareil core (a sugar/starch bead) claimed in the present invention.

Similarly, Van Balken et al. does not teach or fairly suggest a dosage form with a non-

pareil core. Van Balken et al. teaches a delayed release, exploding dosage form wherein after the delayed release coating is removed, the "core" of the dosage form releases the active ingredient. Example 1 of Van Balken et al. describes how a "core" is made: it is made from a cross-linked carboxymethylcellulose and an active agent. Van Balken et al. does not teach a non-pareil core or a controlled release dosage form.

The independent claims as amended require a non-pareil core. Neither Norling et al. nor Van Balken et al. alone or in combination teach or fairly suggest such a claimed core. For at least this reason, no *prima facie* case for obviousness has been set forth in the office action. Withdrawal of the rejection is respectfully requested.

Accordingly, applicants respectfully request that the rejection of claims 1, 2, 4, 5, 20, 25 to 27, 31 to 33, 36 to 40, 47 to 51, and 64 to 66 under 35 U.S.C. § 102(b) as being obvious over the disclosure of Norling et al. in view of van Balken et al. be withdrawn.

Discussion of the secondary considerations of nonobviousness

During the interview, the Examiner and her supervisor requested that the Applicant provide a discussion of the secondary considerations of nonobviousness of the present invention.

Attached are three research publications that post-date the applicant's invention. These publications demonstrate unexpected results and the long felt need in the art for a formulation that releases fluvoxamine over a period of not less than about 12 hours following oral administration.

The three publications describe double blind studies that evaluate the benefits of controlled-release ("CR") fluvoxamine compositions in the treatment of obsessive-compulsive disorder ("OCD"; see Hollander et al. publication) and generalized social anxiety disorder ("GSAD"; Davidson et al. and Westenberg et al. publications).

Davidson et al. reports that treatment with fluvoxamine CR resulted in statistically and clinically significant improvements in symptoms associated with GSAD. In addition, treatment with fluvoxamine CR did not result in weight gain (a side-effect of other SSRIs) or differences in overall sexual function. Accordingly, the conclusion of this study was that fluvoxamine CR was useful in the treatment of GSAD with few side-effects.

Westenberg et al. describes a similar result. Westenberg et al. report that fluvoxamine CR was significantly superior to placebo in decreasing social anxiety scores of subjects. In addition, treatment with fluvoxamine CR did not result in weight gain or differences in overall sexual function. Accordingly, the conclusion of this study was that fluvoxamine CR was useful in the treatment of GSAD with few side-effects.

Hollander et al. investigated the efficacy of fluvoxamine CR in the treatment of OCD. They reported that fluvoxamine CR was associated with a statistically significant and clinically relevant reduction in OCD severity and was found to be safe and well tolerated. Hollander et al. also report that fluvoxamine CR has a significantly earlier onset of therapeutic effects as compared to other SSRIs. The authors surmise that this may be because fluvoxamine CR is a controlled-release formulation with less daily fluctuation in drug concentration which results in patients spending more time each day above the minimal therapeutically effective concentration.

The benefits of using a controlled-release fluvoxamine composition as opposed to an immediate-release fluvoxamine composition are summarized in Hollander et al. (page 641, column 1, second full paragraph):

> The ability to administer fluvoxamine CR once daily may increase patient compliance with long-term therapy, and reduced fluctuations in plasma concentration may be associated with fewer side effects and greater symptom improvement.

Accordingly, the present invention is nonobvious due to secondary considerations.

II. Discussion of the Examiner's Section 103 Rejection of Claims 1, 2, 4, 5, 20, 23 to 34, 36 to 40, 45 to 51, and 55 to 66

The Examiner rejected Claims 1, 2, 4, 5, 20, 23 to 34, 36 to 40, 45 to 51, and 55 to 66 under 35 U.S.C. § 102(b) as being obvious over the disclosure of U.S. Patent No. 5,958,458 to Norling et al. in view of U.S. Patent No. 6,183,780 to van Balken et al. and WO 99/01122 ("Curatolo et al.").

The deficiencies of Norling et al. and van Balken et al. are noted above (different core, different release profile, do not teach a controlled release system of fluvoxamine). Curatolo et al. has been cited for the teaching of release profiles and blood serum levels.

Curatolo et al. provides no disclosure to overcome the deficiencies of Norling et al. and van Balken et al.

In addition, the secondary considerations noted above apply to this obviousness rejection.

Accordingly, applicants respectfully request that the rejection of claims 1, 2, 4, 5, 20, 23 to 34, 36 to 40, 45 to 51, and 55 to 66 under 35 U.S.C. § 102(b) as being obvious over the disclosure of Norling et al. in view of van Balken et al. and Curatolo et al. be withdrawn.

III. Disqualification of U.S. Application No. 10/827,689 as Prior Art under 35 U.S.C. §103(c)

During the Examiner Interview, dated October 3, 2007, the Examiner identified U.S. application No. 10/827,689 ("Devane et al."; published as US20040197405). Devane et al. claims priority to PCT/US99/25632, which published as WO 00/25752 on May 11, 2000. The earliest priority date for Devane et al. is to U.S. provisional application No. 60/106,726, filed November 2, 1998.

The present application claims priority to PCT/IE00/00060, filed May 10, 2000, which claims priority to U.S. provisional application No. 60/135,028, field May 20, 1999. Both of these dates are before the initial publication date of Devane et al. Accordingly, Devane et al. would be prior art under 35 U.S.C. §102(e).

Applicants submit that the present application, U.S. application No. 09/744,169, and Devane et al., U.S. application No. 10/827,689, were, at the time the invention of U.S. application No. 09/744,169 was made, both owned or had an obligation to be assigned to Elan Corp. plc.

Accordingly, under 35 U.S.C. §103(c), applicants respectfully request disqualification of U.S. application No. 10/827,689 as prior art to the present application.

IV. Conclusion

For the reasons expressed above, Applicants request respectfully that the Examiner reconsider and withdraw his rejections. A favorable action on the merits is requested respectfully.

It is hereby requested that the term to respond to the Action, dated May 18, 2007, be extended three months, from August 18, 2007 to November 18, 2007.

Payment to cover the extension fee has been submitted electronically. The Commissioner is hereby authorized to charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 19-5425.

Respectfully submitted,

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